REMARKS

Entry of this Amendment and reconsideration of the subject application in view thereof are respectfully requested.

I. Claims

Claims 1-4 were pending and these claims stood rejected.

Claims 1 and 3 have been amended to clarify the invention. No new matter is added by these amendments.

II. Specification

Applicant respectfully submits that the specification has been amended to claim the benefit of all of the prior-filed applications. No new matter is added by this amendment to the specification.

III. Drawings

The Examiner required a proposed drawing correction of the noted defects in the Notice of the Draftsperson's Patent Drawing Review attached with Paper No. 4. The Draftsperson's Notice indicates that correction of figures/drawings 4A-6, 8, 9A-9C, 10, 12, 13, 13B, 14, 15, 16 are required. Of these, applicant believes that figures 13A, 13B, 14, 15 and 16 as filed with the application comply with the margin requirements under 37 CFR §1.84. Notwithstanding, applicant submits herewith proposed drawing corrections of all of the figures/drawings indicated in the Notice for consideration by the Examiner. Applicant believes that the drawings submitted herewith fully comply with 37 CFR §1.84. Accordingly, should these drawings be deemed formal, Applicant hereby requests that the drawings be forwarded to the Drawing Review Brach along with "Transmittal of Formal Drawings" accompanying this amendment.

IV. Rejection Under 35 U.S.C. § 112 Second Paragraph

Claim 3 stood rejected under 35 U.S.C. § 112, second paragraph, as indefinite because of improper Markush language. Applicant believes that the present claim 3, as amended, obviates

this part of the rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

V. Rejection Under 35 U.S.C. § 103

The Examiner rejected claims 1-4 under 35 U.S.C. § 103(a) as being unpatentable over Goodman et al., 1990, U.S. Patent 4,956,282 in view of Ma et al., 1994, Eur. J. Immunol. **24**:131-138 and Lomonossoff et al., 1999, US Patent 5,874,087. Applicant respectfully traverses this rejection.

Goodman teaches vector constructs for the expression of mammalian proteins in plant cells. "The transfer of the DNA construct into the plant cell may be by infection with *A. tumefaciens* or *A. rhizogenes*, microinjection, liposome fusion, viral infection". Regardless of the particular manner in which the DNA is introduced into the plant cell, the constructs in Goodman are designed for integration into the plant genome for expression of the mammalian proteins. See, for example, column 2, lines 12-21 and column 3, line 65 through column 4, line 33. With respect to viral vectors, Goodman makes clear that "[a] viral system may be employed which provides for integration into the host genome." See, columan 4, lines 41-42. Thus, Goodman teaches large scale production of foreign polypeptides using a transgenic approach contrary to the applicant's claimed approach (i.e., by expressing the genomic component of plant virus vectors without any need for integration into the host genome).

Applicant respectfully disagrees with the Examiner's assertion on page 3 of the Office Action that "Goodman *et al.* Differs from the claimed invention [only] because the production of monoclonal antibodies and the infection of plants (as opposed to plant cells) are not taught." Not only that Goodman's teachings stand in stark contrast to the claimed invention, this refrence does not teach, suggest or contemplate, for example, that

(i) heavy and light chains of a full-length antibody are cloned and expressed independently using two viral vector constructs;

(ii) infecting the host plant at one or more locations with these constructs results in systemic infection in the host plant; and

(iii) the heavy and light chains are assembled into the full-length antibody in the host plant simply by expressing the genomic components of the vector constructs.

Ma teaches assembly of heavy and light chains of a murine monoclonal antibody in transgenic tobacco plants. Again, Ma's approach, like Goodman's, is a transgenic approach and is directly contrary to the approach adopted by the Applicant.

Lomonossoff teaches production of foreign polypeptides including antibodies in plant hosts using viral vectors. While Lomonossoff makes a prophetic reference to antibodies at column 2, lines 6-7, the reference fails to teach or suggest the claimed invention. In particular, this reference does not teach or suggest that heavy and light chains of the antibody are cloned and expressed independently using two viral vector constructs such that these two chains are assembled into a full-length antibody in the host plant. Rather, Lomonossoff teaches or suggests to use modified virus particles such that the foreign peptide is expressed as part of the capsid protein and is produced as part of the whole virus particle. See column 2, lines 49-67. One skilled in the art would know that if the two chains are expressed as part of the capsid protein, then the individual chains do not assemble into a full-length antibody in the virus particle, much less in the host plant without becoming part of the virus particle . Therefore, Lomonossoff does not suggest the claim requirement to express heavy and light chains of an antibody independently using two viral vector constructs wherein the heavy and light chains resulting from the expression are assembled into a full-length antibody in the host plant. Applicant made this possible by placing each of the respective chains under a subgenomic promoter and has shown, by way of a working example (Example 8), that such an approach can be used to produce a full-length antibody in the host plant without becoming part of the virus particle.

Thus, of the three cited references, two (Goodman and Ma) are directly contrary to the Applicant's approach, and the third (Lomonossoff) is not pertinent either on its own or in combination with the other cited references. Therefore, the combination Goodman with Ma and Lomonossoff is nothing more than an indiscriminate combination of the prior art. There is no suggestion or motivation to modify Goodman in light of Ma and Lomonossoff to arrive at the claimed invention for the above reasons. The teachings of the cited references can be combined only if there is some suggestion or incentive to do so. *In re Fine*, 837 F.2d 1071, 5 USPQ2d at

1596, 1599 (Fed. Cir. 1992). The combination of Goodman Ma and Lomonossoff fails to satisfy this requirement.

Even if, *arguendo*, there was some suggestion or motivation to modify Goodman in light of Ma and Lomonossoff as averred by the Examiner, there is no evidence suggesting the modification would be successful because Ma follows transgenic approach and Lomonossoff suggests nothing about how the heavy and light chains of a full-length antibody can be produced without making them part of a virus particle or how the heavy and light chains can be assembled into the full-length antibody in the host plant simply by expressing the genomic components of the viral vectors. For a proper rejection under § 103, in addition to suggesting the claimed invention, the prior art must also have revealed that in so making or carrying out the claimed method, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). The combination of Goodman Ma and Lomonossoff further fail to satisfy this requirement.

Furthermore, Ma successfully demonstrates that heavy and light chains of a monoclonal antibody can be assembled correctly in transgenic plants and suggests that transgenic plants may be suitable for high-level expression of more complex genetically engineered immunoglobulin molecules. See abstract, on page 131, of Ma. A person of ordinary skill, upon reading the Ma reference, would be led in a direction divergent from the approach adopted by the Applicant. Such a reference may be said to teach away. *In re Gurley*, 27 F.3d 551, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). The requisite teaching or suggestion to combine the teachings of the cited prior art references is absent when one of the cited references teaches away from rather than toward the claimed features. *In re Bell*, 991 F.2d 781, 26 USPQ 2d 1529, 1532 (Fed. Cir. 1993). Stated otherwise, the teachings of Ma reference is a *per se* demonstration of lack of *prima facie* obviousness of the claimed invention.

Accordingly, the Examiner's *prima facie* case of obviousness fails. If the Examiner is aware of references which would tend to remedy the shortcomings of Goodman, the Examiner is asked to cite them. If such facts are within the Examiner's personal knowledge, the Examiner is requested to make them part of the record by way of affidavit as required by 37 C.F.R. §1.104(d)(2). In the absence of such additional disclosures, the rejection under §103 is improper. Reconsideration is respectfully requested.

VI. Conclusion

Applicant believes this response to be a full and complete response to the Office Action. Accordingly, favorable reconsideration in view of this response and allowance of all of the pending claims are earnestly solicited.

Respectfully submitted,

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Marked Up Version of Amendments in Serial No. 09/673,174

IN THE SPECIFICATION:

Please replace the paragraph beginning on page 1, line 4 with the following paragraph:

This application is the United States national stage of International Application No. PCT/US99/25566, filed October 29, 1999, which was published under ***PCT Article*** 21 (2) in English as International Publication No. WO 00/25574, and which claims the priority of U.S. Provisional Application No. 60/106,221, filed October 30, 1998.

IN THE CLAIMS:

1. (Amended) A method for producing a full-length antibody in a host plant using a virus, the method comprising:

(a) constructing a first recombinant viral vector for infection which comprises a recombinant genomic component of the virus, said component having a movement protein encoding nucleic acid sequence and a coat protein nucleic acid sequence, and a nucleic acid sequence for the heavy chain of the antibody [cloned into the recombinant genomic component] such that the expression of the recombinant genomic component also results in the expression of the heavy chain of the antibody;

(b) constructing a second recombinant viral vector for infection which comprises the same recombinant genomic component as in step (a) except that said component has a nucleic acid sequence for the light chain of the antibody [is cloned into the recombinant genomic component] instead of the heavy chain such that the expression of the recombinant genomic component also results in the expression of the light chain of the antibody;

(c) infecting the host plant at one or more locations with the first recombinant viral vector and the second recombinant viral vector such that the infection of said plant with the first and second recombinant viral vectors results in systemic infection in the host plant;

(d) expressing the first and second recombinant genomic components, wherein the heavy and light chains resulting from the expression are assembled into the full-length antibody in the host plant.

3. (Amended) The method of claim 1, wherein the full-length antibody is directed to an antigen selected from the group consisting of hepatitis B surface antigen, enterotoxin, rabies virus glycoprotein, rabies virus nucleoprotein, Norwalk virus capsid protein, gastrointestinal cancer antigen, G protein of Respiratory Syncytial Virus, Sandostatin, anthrax antigen [or] and colorectal cancer antigen.